

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-5. (Canceled)

6. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein said antibody comprises complementarity determining regions (CDRs) comprising  
(A) the amino acid sequences of anti-blood coagulation factor IX/IXa antibody H chain CDRs of the following (a1) or (a2) and L chain CDRs of the following (b1) or (b2); and  
(B) the amino acid sequences of anti-blood coagulation factor X antibody H chain CDRs of any one of the following (c1) to (c9) and L chain CDRs of the following (d1) or (d2):

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively;

(a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 18, 19, and 20, respectively;

(b1) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively;

(b2) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(c1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively;

(c2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 26, 27, and 28, respectively;

(c3) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 30, 31, and 32, respectively;

(c4) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 34, 35, and 36, respectively;

(c5) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 38, 39, and 40, respectively;

(c6) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 42, 43, and 44, respectively;

(c7) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 46, 47, and 48, respectively;

(c8) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 50, 51, and 52, respectively;

(c9) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 54, 55, and 56, respectively

(d1) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively;

(d2) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

7. (Previously presented) A composition comprising the antibody according to claim 6 and a pharmaceutically acceptable carrier.

8. (Previously presented) A composition comprising the antibody according to claim 6, wherein said composition is a pharmaceutical composition for treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding.

9. (Original) The composition according to claim 8, wherein the bleeding, disorder accompanied by bleeding, or disorder caused by bleeding is a disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

10. (Original) The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is hemophilia A.

11. (Original) The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is a disorder in which an inhibitor against blood coagulation factor VIII and/or activated blood coagulation factor VIII is generated.

12. (Original) The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is acquired hemophilia.

13. (Original) The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease of blood coagulation factor VIII and/or activated blood coagulation factor VIII is von Willebrand's disease.

14. (Previously presented) A method for treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding, wherein said method comprises the step of administering the antibody according to claim 6.

15. (Canceled)

16. (Previously presented) A kit for treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding, wherein said kit comprises at least the antibody according to claim 6.

17. (Previously presented) A method of treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding, wherein said method comprises the step of administering the antibody according to claim 6 in combination with blood coagulation factor VIII.

18. (Previously presented) A kit for treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding, wherein said kit comprises at least the antibody according to claim 6 and blood coagulation factor VIII.

19. (Previously presented) A method for treating bleeding, a disorder accompanied by bleeding, or a disorder caused by bleeding, wherein said method comprises the step of administering the composition according to claim 7.

20. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody

(A) binds the same epitope of blood coagulation factor IX/IXa as an antibody having the H chain CDRs of (a1) or (a2) below and the L chain CDRs of (b1) or (b2) below, and

(B) binds the same epitope of blood coagulation factor X as an antibody having the H chain CDRs of any one of (c1) to (c9) below and the L chain CDRs of (d1) or (d2) below:

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively;

(a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 18, 19, and 20, respectively;

(b1) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively;

(b2) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(c1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively;

(c2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 26, 27, and 28, respectively;

(c3) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 30, 31, and 32, respectively;

(c4) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 34, 35, and 36, respectively;

(c5) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 38, 39, and 40, respectively;

(c6) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 42, 43, and 44, respectively;

(c7) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 46, 47, and 48, respectively;

(c8) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 50, 51, and 52, respectively;

(c9) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 54, 55, and 56, respectively;

(d1) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively;

(d2) L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

22. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising:

(a) an anti-blood coagulation factor IX/IXa antibody variable region comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213; and

(b) an anti-blood coagulation factor X antibody variable region comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

23. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising anti-blood coagulation factor IX/IXa H and L variable domains comprising a set of six CDR sequences selected from (a1) and (a2) below and anti-blood coagulation factor X H and L variable domains comprising a set of six CDR sequences selected from (b1) and (b2) below:

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively;

(b1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(b2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

24. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising

(A) anti-blood coagulation factor IX/IXa antibody H and L variable domains comprising a set of six CDR sequences selected from (i) and (ii):

(i) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(ii) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively; and

(B) an anti-blood coagulation factor X antibody variable domain comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

25. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising

(A) an anti-blood coagulation factor IX/IXa antibody variable domains comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213; and

(B) anti-blood coagulation factor X antibody H and L variable domains comprising a set of six CDR sequences selected from (i) and (ii):

(i) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(ii) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

26. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising an anti-blood coagulation factor IX/IXa antibody variable domain comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213, wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

27. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising anti-blood coagulation factor IX/IXa antibody H and L variable domains comprising a set of six CDR sequences selected from (a) and (b):

(a) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(b) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

28. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising an anti-blood coagulation factor X antibody variable region comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217, wherein the



antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

29. (Previously presented) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, the antibody comprising anti-blood coagulation factor X antibody H and L variable domains comprising a set of six CDR sequences selected from (a) and (b):

(a) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(b) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

30. (Previously presented) A method of promoting blood coagulation factor X activation by blood coagulation factor IXa, the method comprising contacting a blood coagulation factor X and a blood coagulation factor IXa with the antibody according to claim 6.

31. (Previously presented) A method of promoting coagulation of blood or plasma, the method comprising contacting blood or plasma with the antibody according to claim 6.

32. (Previously presented) The method of claim 31, wherein the blood or plasma is deficient in blood coagulation factor VIII or has a functional reduction in blood coagulation factor VIII activity.

33. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody

(a) binds the same epitope of blood coagulation factor IX/IXa as an antibody having a variable region comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213, and

(b) binds the same epitope of blood coagulation factor X as an antibody having variable region comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

34. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X. wherein the antibody

(A) binds the same epitope of blood coagulation factor IX/IXa as an antibody having H and L variable domains comprising a set of six CDR sequences selected from (a1) and (a2) below, and

(B) binds the same epitope of blood coagulation factor X as an antibody having Hand L variable domains comprising a set of six CDR sequences selected from (b1) and (b2) below,

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively;

(b1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain. CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(b2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively;

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

35. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody

(A) binds the same epitope of blood coagulation factor IX/IXa as an antibody having H and L variable domains comprising a set of six CDR sequences selected from (i) and (ii):

(i) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(ii) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively; and

(B) binds the same epitope of blood coagulation factor X as an antibody having variable domain comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

36. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody

(A) binds the same epitope of blood coagulation factor IX/IXa as an antibody having variable domains comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213; and

(B) binds the same epitope of blood coagulation factor X as an antibody having Hand L variable domains comprising a set of six CDR sequences selected from (i) and (ii):

(i) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(ii) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

37. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody binds the same epitope of blood coagulation factor IX/IXa as an antibody having variable domain comprising the amino acid sequence of SEQ ID NO: 13, 17, 85, 205, or 213, wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

38. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody binds the same epitope of blood coagulation factor IX/IXa as an antibody having H and L variable domains comprising a set of six CDR sequences selected from (a) and (b):

(a) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 214, 215, and 216, respectively;

(b) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 86, 87, and 88, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 206, 207, and 208, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

39. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody binds the same epitope of blood coagulation factor X as an antibody having variable region comprising the amino acid sequence of SEQ ID NO: 21, 25, 29, 33, 37, 41, 45, 49, 53, 161, 209, or 217, wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.

40. (New) A bispecific antibody that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X, wherein the antibody (A) binds the same epitope of blood coagulation factor X as an antibody having H and L variable domains comprising a set of six CDR sequences selected from (a) and (b):

(a) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 218, 219, and 220, respectively;

(b) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 162, 163, and 164, respectively, and L chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 210, 211, and 212, respectively,

wherein the antibody functionally substitutes for blood coagulation factor VIII and/or activated blood coagulation factor VIII.